**CLINICAL OBSERVATIONS**

**Starvation Diets as a Cause of Acquired Long QT Syndrome**

*Background:* Prolongation of the rate-corrected QT interval (QTc) and ventricular arrhythmias have been described in persons on starvation diets (1). Prolongation of the QTc interval as measured by standard 12-lead electrocardiography is an independent risk factor for sudden death due to cardiac arrest (2).

*Objective:* To determine whether long-term weight loss over 7 weeks can influence cardiac repolarization as indicated by the electrocardiographic QT interval.

*Methods:* The electrocardiographic QT, RR, and QTc (QT/RR(0.5)) intervals were assessed in 29 healthy obese (body mass index > 27 kg/m²) persons on a very-low-calorie diet (800 kcal/d) for 7 weeks. The intervals, serum albumin, and electrolytes were measured at baseline, once weekly, and at the end of diet therapy. Twelve-lead electrocardiograms were obtained from all patients in a supine position after 10 minutes at rest. The electrocardiograms were recorded at standard gain (10 mv/mm) and speed (25 mm/s). The QT interval was measured from the onset of the QRS complex to the end of the T wave in all leads in which the end of the T wave could be clearly defined. The QT intervals were corrected for heart rate by using the Bazett formula. Patients with atrial fibrillation, bundle-branch block, and pacemakers were excluded. All patients gave informed consent.

*Results:* The QTc interval before the start of the diet was 0.42 seconds (SD, 0.025) by manual measurement and 0.41 seconds (SD, 0.022) by automated measurement. Of 29 patients, 20 had QTc interval prolongation greater than 0.43 seconds, and 12 had moderate prolongation (>0.45 seconds) at the end of the fast (Table).

*Discussion:* Weight reduction diets may reduce the severity of risk factors for coronary heart disease, such as diabetes, hypertension, and dyslipidemia. However, reports of deaths in patients using variants of low-calorie diets have raised some questions and discussions about the safety of these procedures. In this study, 20 of 29 patients on a very-low-calorie diet had some degree of QTc interval lengthening. The importance of these findings is demonstrated by a patient with QTc lengthening after fasting who had cardiac arrest due to torsade de pointes and was successfully resuscitated (3). Lengthening of the QT interval as a result of a very-low-calorie diet and starvation is of potential clinical importance because it can predispose patients to potentially fatal ventricular arrhythmias, such as torsade de pointes. Prolongation of the QT interval in these situations may be due to biochemical changes in the myocardial membrane, thereby altering potassium flux with prolongation or delay of electrical repolarization (4). Of note, the majority of patients with documented acquired long QT syndrome never experience torsade de pointes, and many patients with torsade de pointes have normal QT intervals shortly before the event. It seems that a variety of coincident circumstances, including genetic predisposition and prolonged QT interval (which may occur precipitously and transiently), is required to precipitate torsade de pointes (5).

Because sudden cardiac death in persons consuming a low-calorie diet has been suggested to relate to repolarization abnormalities, such as QT prolongation, regular careful monitoring with electrocardiography studies might reduce the risk for fatal ventricular arrhythmias and mortality in these patients.

*Conclusion:* Very-low-calorie diets can cause lengthening of the QT interval and increase the risk for sudden death due to cardiac arrest.

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**Table. Correspondence of QTc With Potassium and Serum Albumin Levels**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value at Start of Diet</th>
<th>Value at End of Diet</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean QTc (SD), s</td>
<td>0.42 (0.025)</td>
<td>&lt;0.43 (9 patients)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&lt;0.43 and ≤0.45 (8  patients)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>≤0.45 (12 patients)*</td>
</tr>
<tr>
<td>Potassium level</td>
<td>Normal in all patients</td>
<td>Normal in all patients</td>
</tr>
<tr>
<td>Serum albumin level</td>
<td>Normal in all patients</td>
<td>Normal in all patients</td>
</tr>
</tbody>
</table>

QTc = rate-corrected QT interval.  
* The QTc interval was 0.48 seconds in 4 patients, 0.49 seconds in 2 patients, 0.51 seconds in 2 patients, 0.52 seconds in 1 patient, 0.54 seconds in 2 patients, and 0.55 seconds in 1 patient.
The patient’s baseline electrocardiogram showed normal sinus rhythm with incomplete right bundle-branch block. A dobutamine stress test was performed per standard protocol, and at 40 μg/kg per min, at 70% of maximum predicted heart rate, the patient developed ventricular bigeminy followed by nonsustained ventricular tachycardia accompanied by severe left-sided chest pressure without dyspnea. Electrocardiography revealed 4-mm ST-segment elevations in leads II, III, aVF, and V2 through V6 and ST-segment depressions in leads I and aVL.

Emergent cardiac catheterization showed mild nonobstructive coronary artery disease but marked apical dyskinesis on left ventriculography (Figure). A transthoracic echocardiogram showed normal chamber sizes and thickness with hyperkinetic basal segments, akinesis of the apical segments, systolic anterior motion of the mitral valve leaflets, and a late-peaking left ventricular outflow tract gradient of 50 mm Hg. The troponin I level peaked at 7 μg/L. Norepinephrine and dopamine levels obtained 2 hours after the onset of chest pain were 5745.5 pmol/L (normal, <4433 pmol/L) and 835.6 pmol/L (normal, <195.8 pmol/L), respectively. Cardiac magnetic resonance imaging 3 days after admission demonstrated akinesis of the left ventricular apex with no significant late gadolinium enhancement. The patient did not report any recent stressors or new medications. She was treated with aspirin, simvastatin, carvedilol, and anticoagulation to prevent apical thrombus. After 2 days, the patient was free of chest pain and the electrocardiogram had returned to normal. Repeated echocardiography after 1 week demonstrated marked improvement in left ventricular wall motion, with resolution of left ventricular outflow tract gradient.

Discussion: The pathophysiology of transient apical ballooning syndrome is incompletely understood and is thought to result from acute psychological or medical stress leading to transient dysfunction of the left ventricular apex (1). It is unknown whether the transient left ventricular dysfunction is due to microvascular spasm, stunned myocardium, or heightened adrenergic activation of the apex caused by differential concentration of β-receptor density. Because our patient lacked a known preceding psychological stressor, it is conceivable that dobutamine, given its sympathomimetic properties, may have been the precipitant. Several other case reports document similar responses to dobutamine (2–4).

Conclusion: Dobutamine may precipitate transient apical ballooning syndrome. We alert clinicians to the possibility of this complication of dobutamine stress testing so that the syndrome can be rapidly recognized and appropriately treated.

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References

Metoclopramide as a Possible Cause of Prolonged QT Syndrome and Torsade de Pointes in a Patient With Heart Failure and Renal Insufficiency

Background: The long QT syndrome is a disorder of myocardial repolarization characterized by a prolonged QT interval and is associated with an increased risk for torsade de pointes. Metoclopramide is known to block ion channels, causing QT interval prolongation in experimental situations, but this has rarely been described in humans.

Objective: To describe a patient with heart failure and renal impairment who was receiving metoclopramide and developed prolonged QT and torsade de pointes.

Case Report: An 86-year-old man with a history of hypertension was admitted to the hospital after 6 weeks of shortness of breath. His history included gastroesophageal reflux disorder and hypothyroidism. His medications were l-thyroxine, metoclopra-
mide, and lisinopril. On examination, he was in decompensated heart failure with an elevated jugular venous pulse, bibasilar rales, and pitting pedal edema. He had normal electrolyte levels (sodium, 136 mmol/L; potassium, 4.4 mmol/L; magnesium, 2.3 mmol/L [2.3 mEq/L]), thyroid function (thyroid-stimulating hormone level, 4.4 mU/L), and myocardial enzyme levels. The electrocardiogram (ECG) (Figure A) on admission showed normal sinus rhythm and normal rate-corrected QT interval (QTc) (410 ms). He was given furosemide and continued receiving metoclopramide, 10 mg 4 times daily. The day after admission, his creatinine level increased from 14.92 μmol/L (1.3 mg/dL) to 167.96 μmol/L (1.9 mg/dL). A repeated ECG (Figure, B) showed prolongation of QTc (597 ms). In the next couple of hours, he developed torsade de pointes (Figure, C), which was successfully defibrillated. A repeated electrolyte check showed a magnesium level of 1.8 mmol/L (1.8 mEq/L), potassium level of 3.7 mmol/L, and troponin level of 0.00014 μg/L. He continued to have pause-dependent torsade de pointes on 3 more occasions, requiring defibrillation. After the events, the patient had coronary angiography, which showed normal coronary arteries. He received no further doses of metoclopramide, and the ECG showed reversion to a normal QT interval.

Discussion: The blocking of the human ether-à-go-go–related gene–encoded outward K⁺ current channel is thought to be the main cause of most cases of drug-induced long QT syndrome (1). Metoclopramide blocks the receptors in experimental models (2). The long QT syndrome after administration of metoclopramide in persons without underlying conduction abnormalities has not been reported (3).

Our patient had a normal QT interval at admission but developed QT prolongation the next day at the time of transient impairment of renal function due to worsening heart failure. We excluded myocardial ischemia and electrolyte abnormalities as causes; acute myocarditis could have been a cause, but the patient had had symptoms of heart failure for 6 weeks and had a normal ECG, normal heart rate, and normal cardiac enzyme levels at admission. A case report describes torsade de pointes after administration of metoclopramide in a patient with underlying complete left bundle-branch block (3). Because 80% of metoclopramide excretion occurs through the kidneys, we speculate that accumulation of the drug in the context of heart failure and renal insufficiency contributed to this patient’s long QT syndrome and torsade de pointes, an impression supported by the observation that the ECG became normal after metoclopramide was withheld.

Conclusion: Metoclopramide seemed to contribute to the long QT syndrome and torsade de pointes in a patient with heart failure and renal insufficiency.

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PVB = premature ventricular beat; QTc = rate-corrected QT interval. A. The electrocardiogram on admission shows normal QTc of 410 ms. B. The electrocardiogram 24 hours after admission shows prolonged QTc of 597 ms with diffuse T wave inversion in precordial leads. C. Sinus bradycardia with a PVB (single asterisk), then a “short-long-short” sequence followed by another PVB (double dagger), inducing torsade de pointes.

Figure. Electrocardiograms with normal and prolonged QTc.
Corrections

Correction: Clinical Implications of Short-Term Variability in Liver Function Test Results

On page 349 of our article (1), the second paragraph of the Measurements section says “. . . we defined elevated liver test results as . . . alkaline phosphatase levels higher than 177 U/L . . . ” It should say “. . . we defined elevated liver test results as . . . alkaline phosphatase levels higher than 117 U/L . . . ”. We verified that all results and analyses used correct values.

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Reference

Correction: In The Clinic: Alcohol Use

In the last paragraph on page ITC3-10 of the In The Clinic on Alcohol Use (1), diazepam is incorrectly listed as a short-acting agent, and oxazepam is incorrectly listed as a long-acting agent. Diazepam should be listed as a long-acting agent, and oxazepam should be listed as a short-acting agent.

Reference